IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Stephen Quirk

Title: MODULAR PEPTIDE-BASED REAGENT

Docket No.: 1443.026US1
Filed: December 20, 2001
Examiner: Michael L. Borin
Customer No.: 21186

Serial No.: 10/027038
Due Date: September 27, 2003
Group Art Unit: 1631
Confirmation No.: 2238

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

We are transmitting herewith the following attached items (as indicated with an "X"):

X A return postcard.
X An Response to a Restriction Requirement (3 Pages).

If not provided for in a separate paper filed herewith, Please consider this a PETITION FOR EXTENSION OF TIME for sufficient number of months to enter these papers and please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
Customer Number 21186

By: Robin A. Chadwick
Atty: Robin A. Chadwick
Reg. No. 36,477

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O.Box 1450, Alexandria, VA 22313-1450, on this 26 day of September, 2003.

Gina Upshaw
Name

Gina Upshaw
Signature

SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A. Customer Number 21186
(GENERAL)

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RESPONSE TO RESTRICTION REQUIREMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia, 22313-1450

Applicant has reviewed the Restriction Requirement mailed August 27, 2003 and provisionally elects, with traverse, the claims of Group III (claims 14-28), and amino acid sequence SEQ ID NO:11.

The Restriction Requirement is traversed on the basis that Restriction Requirements are optional in all cases. M.P.E.P. § 803. If the search and examination of an entire application can made without serious burden, the Examiner must examine it on the merits, even though it arguably may include claims to distinct or independent inventions. M.P.E.P. § 803. It is respectfully submitted that the search and examination of the claims can be made without serious burden on the Office. Thus, reconsideration and withdrawal of the Restriction Requirement is respectfully requested.

The Examiner has indicated that for each of Groups I-III, an election of a nucleic acid or amino acid sequence must be made. Applicants elect, with traverse, SEQ ID NO:11 for examination at this time. The Examiner has stated that this is not a species election.

Applicant respectfully traverses the election of sequence associated with the election of Group III. The number of sequences claimed in this group of claims is few in number; *i.e.*, only ten sequences (SEQ ID NO:2-6, 8-11 or 14). Moreover, Applicant submits that the subject matter of the sequences claimed are related and a search of all SEQ ID NO:2-6, 8-11 and 14 would not constitute a burden. As described in the specification at pages 13-14.

The sequence of wild-type APP is as follows SEQ ID NO:1):

GPSQPTYPGD DAPVEDLIRF YDNLQQYLNV VTRHRY

In contrast to the APP sequence, the peptide backbones of the invention are modified in order to engineer a molecule that is more

In contrast to the APP sequence, the peptide backbones of the invention are modified in order to engineer a molecule that is more useful for diagnostic applications. Residues altered to form one example of a peptide backbone of the invention are shown in bold within SEQ ID NO:1 above. In one embodiment, Tyr27 was substituted with Trp (SEQ ID NO:2, GPSQPTYPGD DAPVEDLIRF YDNLQQWLNV VTRHRY). This amino acid substitution improves packing within the hydrophobic core and also provides a useful intrinsic spectroscopic probe. In another embodiment, Gly1 was changed to Met-Cys (SEQ ID NO:3, MCPSQPTYPGD DAPVEDLIRF YDNLQQYLNV VTRHRY) This alteration allows the molecule to be produced using recombinant methodology, where an initiating Met is required for transcription and translation in *E. coli*. In another embodiment, a Cysteine residue is added at position 30 (replacing Val30) to form a stabilizing disulfide bond with the Cysteine added at the N-terminus (SEQ ID NO:4, MCPSQPTYPGD DAPVEDLIRF YDNLQQYLNC VTRHRY). In another embodiment, Asp11 was replaced with Pro in order to form a more stable kink to the interhelical loop domain and as a way of introducing a unique Sma I site into a nucleic acid encoding the peptide backbone (SEQ ID NO:5, GPSQPTYPGD PAPVEDLIRF YDNLQQYLNV VTRHRY). Similarly Ala12 can be altered to Gly in order to provide a Sma I site in a nucleic acid encoding the peptide backbone (SEQ ID NO:6, GPSQPTYPGD DGPVEDLIRF YDNLQQYLNV VTRHRY). The sequence RHRY (SEQ ID NO:7) can be removed from SEQ ID NO:1, as this sequence has been implicated in APP receptor binding. After removal of RHRY (SEQ ID NO:7), two alanine residues can be added in order to properly space and orient the terminal cysteine residue (SEQ ID NO:8, GPSQPTYPGD DAPVEDLIRF YDNLQQYLNV VTAA). A C-terminal Cys can be added to sequester and properly orient the peptide backbone onto gold or another solid support or surface that forms part of a diagnostic device (SEQ ID NO:9, GPSQPTYPGD DAPVEDLIRF YDNLQQYLNV VTRHRYC; or (SEQ ID NO:10, GPSQPTYPGD DAPVEDLIRF YDNLQQYLNV VTC).

Such sequence changes have been used to generate a 35 amino acid peptide backbone with amino acid sequence SEQ ID NO:11 (**MC**PSQPTYPGD **PG**PVEDLIRFYDNLQQ**W**LN**C**VT**AAC**) . In another embodiment of the invention, the peptide backbone does not have the initial methionine. Instead, the peptide has SEQ ID NO:14 (**C**PSQPTYPGD **PG**PVEDLIRF YDNLQQ**W**LN**C** VT**AAC**) .

Thus, a search and examination of all of SEQ ID NO:2-6, 8-11 or 14 can be made without serious burden on the Examiner.

The Examiner is invited to contact Applicant's Representatives at the below-listed telephone number if there are any questions regarding this Response or if prosecution of this application may be assisted thereby.

Respectfully submitted,

STEPHEN QUIRK PH.D.

By his representatives,

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Date Sept. 26, 2003 By Robin A. Chadwick
Robin A Chadwick
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Gina Uphus
Name

Gina Uphus
Signature